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URINARY SYMPTOMS IN PARKINSON'S DISEASE

Prevalence and associated factors

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ABSTRACT - The authors present a cross-sectional study involving 61 patients with idiopathic Parkinson's disease (PD) who were consecutively examined and compared to a control group with 74 subjects. Only patients who fulfilled the standard diagnostic criteria for PD and whose brain magnetic resonance imaging was normal were included. The objective of the study was to evaluate the prevalence of inferior urinary tract symptoms in PD and to study the possible association between clinical factors to urinary dysfunction. In the patient group, 39.3% presented urinary symptoms when compared to 10.8% in the control group. All symptomatic patients presented irritative symptoms. The most common irritative symptom PD was nocturia, followed by frequency and urinary incontinence. Around 25% of the patients presented functional obstructive symptoms determined by the disease. The most frequent obstructive symptom was incomplete emptying of the bladder. Only the age of the patients and control group were correlated with urinary dysfunction.

KEY WORDS: Parkinson's disease, urinary symptoms, autonomic symptoms.

Prevalência e fatores associados aos sintomas urinários na doença de Parkinson

RESUMO - Trata-se de estudo clínico transversal, envolvendo 61 pacientes com doença de Parkinson idiopática (DP) examinados consecutivamente e comparados a 74 indivíduos do grupo controle. Foram incluídos apenas pacientes com DP que preencheram os critérios de diagnóstico estabelecidos. A ressonância magnética do encéfalo e a ultra-sonografia da próstata foram utilizadas como critérios de exclusão. O objetivo do estudo foi avaliar a prevalência de sintomas do trato urinário inferior na DP e verificar associações entre sexo, idade e fatores clínicos às disfunções urinárias. Sintomatologia urinária foi encontrada em 39,3% dos parkinsonianos e 10,8% do grupo controle. Todos os pacientes sintomáticos apresentavam sintomas irritativos e 25% destes tinham sintomas obstrutivos. A sintomatologia urinária não estava associada ao sexo, duração e gravidade da doença, hipotensão postural e sintomas ortostáticos, assim como com os sinais cardeais e tratamento com a levodopa.

PALAVRAS-CHAVE: doença de Parkinson, sintomas urinários, sintomas autonômicos.

The presence of autonomic alterations in Parkinson's Disease (PD) could influence the diagnosis and prognosis of the disease. In 1817, James Parkinson reported the presence of autonomic signs such as sudoresis, urinary and gastrointestinal symptoms[1]. The lower urinary tract symptoms (LUTS) are classified in irritative and obstructive symptoms. In the irritative group, there are frequency, urgency and nocturia which are caused by hyperactivity of the bladder due to detrusor hyperreflexia. Incomplete emptying, intermittence, weak urinary stream and hesitation are obstructive symptoms. The majority of LUTS found in PD are irritative. Obstructive symptoms or both irritative and obstructive are less frequently found[2,3]. Detrusor hyperreflexia means a hyperactive bladder due to central nervous system mechanisms. Neurological disorders frequently associated with detrusor hyperreflexia are cerebrovascular disorders, dementia, multiple sclerosis, brain tumor and parkinsonism[4] . According to epidemiological studies of urinary disorders related by Martins Jr. and D'Ancona 9% of the patients with urinary incontinence had

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PD[5].The frequency of urinary symptoms in patients with PD revised by Araki and Kuno varied from 37 to 70%[3]. The distortions in these studies include problems in selecting patients, inclusion of patients with other forms of parkinsonism, the identification of urinary symptoms and the use of medication such as levodopa[3,6]. Bladder hyperactivity in PD patients can be explained by the removal of inhibitory effects exerted by dopamine neurons, originated in the "pars compacta" of the substantia nigra and mediated by D1 receptors, on the urinary reflex[6,7]. The presence of Lewy bodies in the autonomic nervous system of patients with advanced PD can explain urinary sphincter dysfunction and rare cases of hyporeflexia of the detrusor muscle[3].

LUTS can be measured by using the score scale of the American Urological Association (AUA – 7). This scale is a questionnaire of 7 items which was developed to measure the severity of LUTS among men who have prostate hypertrophy[8]. It quantifies the urinary symptoms and has correlation with urodynamic findings even in patients without prostate alteration or in females. It can also measure and differentiate the irritative and obstructive symptoms[8,9]. Patients who have total scores ≥ 8 or irritative scores ≥ 4 and obstructive scores ≥ 5 are considered symptomatic[8].

The objective of this study was to analyze the prevalence of LUTS in PD and to study the possible association of sex, age and clinical factors to urinary disorders.

METHOD

The study was comprised of 61 patients selected from 169 patients with PD who were attended consecutively at the neurological outpatient clinic of Lineu Araujo – SUS Teresina – PI. The control group (74 subjects) was made up of spouses, family and caretakers. Only patients with idiopathic PD who fulfilled the criteria for the established diagnosis were included. Secondary parkinsonism and other types of degenerative parkinsonism were excluded. A brain MRI was done on all participants as exclusion criteria. Patients with dementia, early or severe postural instability, men with prostate hypertrophy or previous prostatectomy and pelvic surgery in women were also excluded. All of the patients were examined after being off levodopa or other dopaminergic medication for 15 hours.

The Unified Parkinson's Disease Rating Scale (UPDRS) and the Hoehn-Yahr scale were used for neurological evaluation. The urinary symptoms were evaluated by AUA-7 scale, which was applied with assistance of the same examiner (RNCS).

An analytic and observational cross-sectional study was conducted. For descriptive analysis, frequency tables, position and dispersion measurements were used. For the study of association between the variables, the Pearson correlation test was used. The statistic T of Student and the variance analysis (ANOVA) were used to compare the mean scores between the groups. The exact Fisher test was used to study the proportions. The significance level used was 5%.

RESULTS

Sex difference and age - In the patient group 31 (50.8%) were male and 30 (49.2%) female, in the control group 31 (41.9%) were male and 43 (58.1%) female. A significant difference between total ($p=0.529$) irritative ($p=0.94$) and obstructive ($p=0.053$) mean urinary scores for men and women with PD was not observed (Table 1). In Table 2, the mean urinary scores were compared between women with PD and women in the control group and a significant difference between total ($p<0.001$), obstructive and irritative mean urinary scores was observed. The average age of the group of patients (PD) was 59.6 years. For men, the ages varied from 36 to 77 years with the mean age of 57 and for women the ages varied from 40 to 82 years with mean age of 62 years. In the symptomatic group the ages varied from 40 to 77 years, with mean age of 62.2 years. In the control group the average of age was 59.3 years.

In the PD group a correlation between age and total urinary scores ($r=0.351$; $p=0.0027$) and between age and irritative urinary scores ($r=0.348$; $p = 0.0029$) was observed. There was no correlation between age and obstructive symptoms ($r= 0.197$; $p= 0.0635$). For the control group there was a clear correlation between age and total urinary scores ($r= 0.46$; $p<0.001$).

Table 1. Mean urinary scores (AUA-7) between the groups.

Groups	N	AUA - 7		
		Total	Irritative	Obstructive
PD	61	7.1	5.2	1.9
Control	74	3.8	2.7	1.1

Table 2. Mean urinary scores (AUA-7) between women groups.

Women Groups	N	AUA - 7		
		Total	Irritative	Obstructive
Control	43	3.1	2.5	0.6
PD	30	6.7	5.2	1.5

Table 3. Prevalence of urinary symptoms between the groups.

LUTS	PD		Controls		
	N	%	N	%	P
Nocturia	39	63.9	21	32.8	< 0.001
Frequency	22	36.1	7	10.9	< 0.001
Urgency	20	32.8	6	9.4	< 0.001
Incomplete emptying	11	18.0	0	0	< 0.001
Intermittence	8	13.1	3	4.69	NS
Weak urinary stream	6	9.8	10	15.6	NS
Hesitation	1	1.6	1	1.56	NS

Comparing groups - There was a significant difference between total ($p<0.0001$) irritative ($p<0.0001$) and obstructive ($p<0.0001$) mean urinary scores of PD patients and control group. In the group of patients studied, we found 24 patients with total urinary scores ≥ 8, corresponding to 39.3% of the total. All of the symptomatic patients had irritative symptoms and 25% of them also had obstructive symptoms.

In Table 3 there were significant differences between nocturia ($p<0.001$), diurnal frequency ($p<0.001$), urgency ($p<0.001$), and incomplete voiding ($p<0.001$), when the patients group was compared to the control group.

Duration and severity - The duration of PD varied from 3 months to 20 years, with mean of 4.9 years and median of 3 years. In the symptomatic patients, the duration of disease varied from 1 to 11 years with mean of 4.5 years. No association between the duration of the disease and total ($r=-0.004$; $p=0.48$), irritative and obstructive urinary scores was observed.

The severity of PD in the sample studied was measured by using the UPDRS scores. The UPDRS total scores varied from 12 to 98 with mean of 45.8, median of 41 and standard deviation of 22. Among the group of symptomatic patients, the mean total scores was 51.6 while in the non-symptomatic group the mean was 42. No significant difference between the mean total scores ($p=0.097$) of symptomatic and non-symptomatic PD patients was observed. In Table 4, the mean scores of the cardinal motor symptoms (UPDRS) were distributed between patients with and without urinary symptoms. No difference was observed in the mean motor scores of tremor ($p=0,255$), rigidity ($p=0,255$) and akinesia ($p=0,229$) between patients with or without symptoms. In Table 5, the mean scores of each section (UPDRS) of PD patients with and without urinary symptoms were compared and no significant difference between the mean scores for *sector I*-mental health, behavior and humor ($p=0.73$), *sector II*-daily activities ($p=0.86$) and *sector III*- motor functions ($p=0.119$) was observed. No correlation between the total points of the UPDRS and the total urinary scores ($r=0.14$; $p=0.136$) was observed. The possible associations of each cardinal motor symptom with total urinary scores were also studied: tremor ($r=0.062$; $p=0.315$); rigidity ($r=0.044$; $p=0.367$) and akinesia ($r=0.069$; $p=0.296$). No correlation between the motor cardinal symptoms and urinary symptoms was found.

Table 4. Mean motor scores (UPDRS) between symptomatic and non-symptomatic PD patients.

Patients	Cardinal symptoms		
	Tremor	Rigidity	Akinesia
Symptomatic	6.67	6.45	18.80
Non- symptomatic	5.56	5.51	16.30

Table 5. Distribution of mean UPDRS scores between symptomatic and non-symptomatic patients.

PD patients	UPDRS		
	Sector I	Sector II	Sector III
Symptomatic	1.83	12.62	37.2
Non-symptomatic	1.73	9.27	31.08

Orthostatic symptoms and postural hypotension - Significant difference between the mean total urinary scores of PD patients with or without orthostatic symptoms ($p=0.948$) and with or without postural hypotension ($p=0.76$) was not observed.

Arterial hypertension - Total (p=0.080), irritative (p=0.084) and obstructive (p=0.352) urinary scores between hypertensive and normotensive PD patients were compared and no difference was observed.

Levodopa - There was no significant difference among total (p=0.831), irritative (p=0.473) and obstructive (p=0.377) mean urinary scores of patients who were treated with levodopa and those treated without levodopa.

DISCUSSION

The identification, in the initial phase of parkinsonism, of autonomic symptoms such as urinary symptoms could influence the diagnosis, treatment efficacy and life quality. However, there have been few studies done on the prevalence of LUTS in patients included with established criteria for PD diagnosis from neurological clinics. The majority of the urological studies on PD evaluated patients that had been sent to urological outpatient clinics with LUTS, which biased the selection. The treatment of urinary symptoms in PD patients is sometimes unsuccessful because LUTS could have neurological origin or be a result of drugs such as levodopa or dopaminergic agents and, particularly in men, it could be associated with structural factors like prostate hypertrophy[3,10,11].

When we compared the mean urinary scores between the PD patients and control group the prevalence of urinary dysfunction determined by PD was significant. In this study, the symptomatic patient was 39.3% against 10.8% of non-symptomatic patients. All the symptomatic patient had irritative symptoms and 25% of them also had obstructive symptoms. The prevalence of symptomatic patients in past studies varied from 27% to 75%[3,10,12]. This variation probably occurs due to the bias selection in urological clinics[11,13] or inclusion of other kinds of parkinsonism[3]. Lemack et al. related that patients with PD would have more contact with physicians, which could influence the questionnaire answers[10]. As the control group was made up of spouses, family and caretakers they had the same health information and the same access to health care.

The PD group urinary scores were compared by gender and no significant difference between total and irritative AUA-7 scores was noted. This suggests that LUTS were not related to sex, which is in agreement to previous studies[3,10]. There was no significant difference between mean obstructive scores for both women and men in the same groups. The prevalence of obstructive symptoms in men caused by prostate and urethral disease could difficult the evaluation of the results in PD patients[5]. Probably this was not observed in the groups studied because men with prostate hypertrophy and previous prostatectomy were excluded. To avoid this kind of distortion women, both from PD and control group, were compared and there was significant difference. This reinforces the evidence that urinary dysfunction either irritative or obstructive are related to the disease[12]. Obstructive urinary symptoms could be explained by sphincter and/or somatic pelvic muscle dysfunction. Galloway reported that the bradykinetic external sphincter was responsible for the obstructive symptoms[14]. More recently this opinion was questioned by Myers et al.[15]. In the PD group a correlation between age and total and irritative scores was observed. In the control group, total, irritative and obstructive urinary scores were strongly associated with age. In cross-sectional studies such as this, we can only infer that urinary dysfunction is age-associated and not an age effect[13].

In the sample studied the duration of PD was not correlated with its severity, specifically motor symptoms severity. There was no association between duration and urinary symptoms. These facts could be explained by different ages at the onset of the disease according to Diamond et al.[16]. By using UPDRS, it was possible to quantify severity and clinical aspects of the disease such as mental state, daily life activity and motor function. Only daily life activity was weakly associated with total urinary symptoms. No difference was observed in the mean total scores of the UPDRS, between symptomatic and non-symptomatic patients suggesting that urinary symptoms were not correlated with severity of the disease. Araki et al. whose studies were based on the Hoenh-Yahr scale and urodynamic methods concluded that urinary function could become progressively worse with PD deterioration[3].

The possible correlation between the presence of autonomic symptoms and LUTS in the patients with PD was studied. The variables studied were the presence of symptoms when in orthostatic position such as: dizziness, blurred vision, syncope and postural hypotension. The presence of these autonomic symptoms studied separately in PD patients was not correlated to urinary symptoms. The urinary scores of hypertensive and normotensive PD patients were compared, and no significant difference was observed, which agrees with the study of Koskimaki et al.[17].

Differences in the urinary symptomatology between those who used and those who did not use levodopa were not found. The simultaneous use of

two or more drugs such as levodopa, anticholinergic agents and dopaminergic agonistics, could potentially cause LUTS, which limits the possibility of studying the role of each one separately[3,11].

CONCLUSION

Lower urinary tract symptoms were prevalent in 39% of the patients in our study. All the symptomatic patients presented irritative symptoms and 25% also presented functional obstructive symptoms. The most frequent irritative symptoms were nocturia followed by frequency and urinary urgency. The most frequent obstructive symptom was incomplete emptying. Sex, duration and severity of the disease, autonomic symptoms represented by postural hypotension and orthosthatic symptoms, the cardinal symptoms (tremor, bradykinesia and rigidity) and levodopa treatment were not associated with urinary symptoms.

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